TABLE I. Patient and Disease Features

	Patient no.			
Parameter	1	2	3	4
Age (years)	58	70	74	60
Gender	Female	Female	Male	Male
Hemoglobin (12–14 g/dl)*	10.7	8.6	11.7	9.0
Marrow plasma cells (%)	50	60	45	90
Serum monoclonal protein (g/l)	56	75	71	65
Myeloma protein type	IgGκ	IgGκ	IgAλ	IgA
Serum creatinine (0.5–1.2 mg/dl)	0.96	0.9	1.3	1.7
Serum albumin (35–50 g/l)	38	32	40	32
Serum calcium (8–10 mg%)	8.9	9.2	10.0	8.9
Serum phosphorus (3.5–5.5 mg%)**	9.5–11	20–27.4	12.3–15.7	9.6–10.2

*Parentheses include normal values.
**Range of three separate measurements.

temia due to hemolyzed sample, hyperlipidemia, or hyperbilirubinemia was excluded.

There was a correlation between the amount of monoclonal protein and the degree of hyperphosphatemia (Table I). In patients 2 and 3, a single large volume plasmapheresis was performed with the use of a continuous flow cell separator. After this procedure, both serum monoclonal protein and phosphorus levels were markedly reduced. After completion of staging procedures, all patients received combination chemotherapy. In patients 1, 2, and 4, an at least 50% reduction of monoclonal protein was noted along with resolution of hyperphosphatemia. Patient 3 did not respond to treatment, and the hyperphosphatemia persisted until his death.

A handful of patients with multiple myeloma and unexplained hyperphosphatemia has been reported [2–5]. This abnormality is thought to be secondary to an increased binding by the monoclonal protein and to a subsequent interference of this complex with the function of the automatic analyzer used to measure serum phosphorus. Increased binding of phosphorus to the monoclonal globulin is likely in our patients since treatment with plasmapheresis in two patients resulted in a marked reduction of both serum monoclonal globulin and phosphorus. Furthermore, serum phosphorus became normal in all three patients responding to chemotherapy.

We conclude that hyperphosphatemia in patients with high levels of monoclonal globulin appears to be spurious and is not associated with any clinical sign. This phenomenon should be recognized so that, in a hyperphosphatemic patient with myeloma without clinical signs of hyperphosphatemia and with normal serum calcium and creatinine levels, no further workup is conducted. Furthermore, the discovery of hyperphosphatemia should trigger measurement of serum globulin to rule out the possibility of a dysproteinemia.

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Subclinical Auditory and Visual Involvement During Oral Deferiprone Therapy

To the Editor: The chronic transfusion program in patients with β thalassemia major is associated with iron overload following organ damage. The recent introduction of an orally active iron chelator, deferiprone (1,2-dimethyl-3-hydroxypyridin-4-one) [1–3], allows us to overcome some obstacles observed during parenteral desferrioxamine (DFO) therapy, such as poor compliance and toxicity involving also the nervous system [4]. Five patients, age ranging 11–31 years (mean age 21.4), were enrolled in this study after giving their or their parents' written informed consent for no compliance to parenteral treatment. Deferiprone was administered in a dose of 70 mg/kg/day (in three split doses). In the basal condition, evaluation of visual and auditory functions as well as neurological examination were found normal in all subjects. The serum ferritin levels in the entire population ranged 2,800–4,659 μg/l.

Brain stem auditory evoked potential (BAEP) to monaural alternate click stimulation, visual evoked potential (VEP) to pattern reversal of 15′ and 55′ checks, and electroretinogram (ERG) were recorded before start of therapy and then every 2 months, for an observation period of 6 (three patients) to 8 (two patients) months of deferiprone therapy. In two of five patients no changes in evoked potential (EP) patterns were observed. During the monitoring of drug effects, BAEPs became altered after a 2-month treatment with a delayed I–III interpeak latency (IL) and remained unmodified at the following recording sessions. In the remaining patient, who presented BAEP alterations before therapy consisting of a prolonged I–III IL, a progressive worsening of tracings with an associated I–V IL was evident. VEPs in two of three patients became abnormal after 4 months from the beginning of deferiprone therapy, with a delayed P100 latency and an abnormal intereye difference. In one case a concomitant alteration of ERG was noted. Visual acuity and audiometric and neurological examinations performed before each recording session were always normal. The mean ferritin concentration, measured monthly in the two patients without EP alterations, decreased progressively, with a decrement of 22.27%,

whereas in the remaining three patients with abnormal EPs, no change or a slight increase was observed.

These preliminary data, although based on few subjects, show a subclinical involvement of the acoustic and visual pathways during deferiprone therapy. The alterations of BAEPs seem to be more precox than those of VEP and show a central involvement. Impairment of the visual pathway seems to be more complex since it is the result of central (papillomacular fibers) and peripheral involvement.

Although presently no data are available on the toxic effects of deferiprone on the nervous system, our results are in accordance with experimental evidence in rats showing changes in ERG similar to those caused by DFO therapy [5].

Our purpose is to continue the EP monitoring in a larger population of thalassemic patients to examine the temporal pattern of these alterations and to clarify the possible mechanisms underlying this subclinical involvement.

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